

## AMENDMENT TO THE CLAIMS

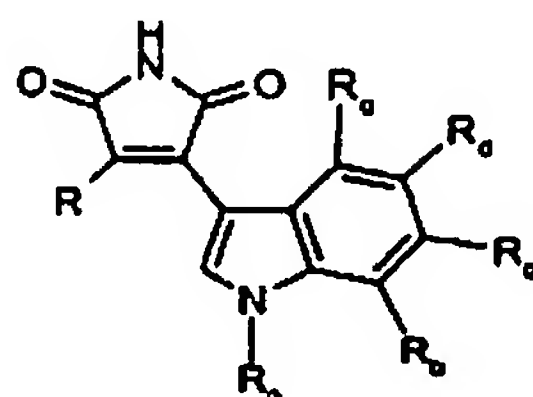
Claim 1. (Canceled)

Claim 2. (Withdrawn): A compound which is an inhibitor of the PKC, in free form or in a pharmaceutically acceptable salt form, wherein said compound possesses a selectivity for the PKC over one or more protein kinases which do not belong to the CDK-family, and a selectivity for the PKC $\alpha$ , PKC $\beta$  and optionally PKC $\theta$ , over one or more of the other PKC isoforms of at least 10 fold, as measured by the ratio of the IC<sub>50</sub> of the compound for a PKC which is not  $\alpha$  and  $\beta$ , and optionally not  $\theta$ , to the IC<sub>50</sub> of the compound for the PKC $\alpha$ , PKC $\beta$  or PKC  $\theta$ , respectively.

Claim 3. (Withdrawn):.A compound which is an inhibitor of the PKC, in free form or in a pharmaceutically acceptable salt form, wherein said compound possesses a selectivity for PKC $\alpha$ , PKC $\beta$  and optionally PKC $\theta$ , over one or more of the other PKC isoforms of at least 10 fold, and for which the ratio of the IC<sub>50</sub> value as determined by Allogeneic Mixed Lymphocyte Reaction (MLR) assay to the IC<sub>50</sub> value as determined by Bone Marrow proliferative (BM) assay is higher than 5.

Claim 4. (Withdrawn): A compound which is an inhibitor of the PKC, in free form or in a pharmaceutically acceptable salt form, wherein said compound possesses a selectivity for the PKC $\alpha$ , PKC $\beta$  and PKC $\theta$ , over one or more of the other PKC isoforms of at least 10 fold, as measured according to claim 2.

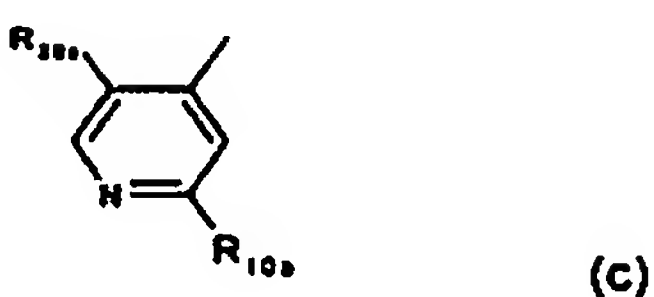
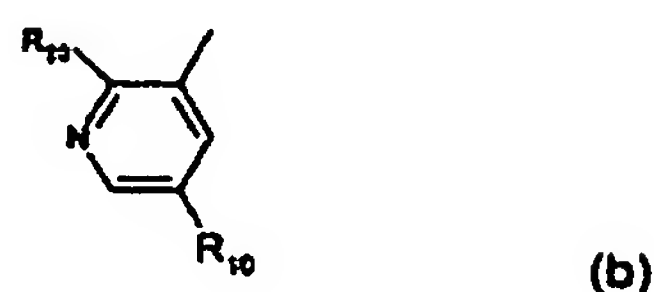
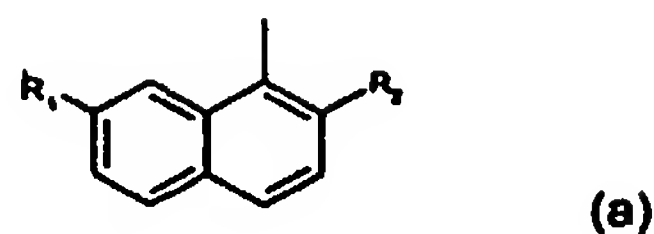
Claim 5. (Previously presented): A compound of formula I



wherein

R<sub>a</sub> is H; C<sub>1-4</sub>alkyl; or C<sub>1-4</sub>alkyl substituted by OH, NH<sub>2</sub>, NHC<sub>1-4</sub>alkyl or N(di-C<sub>1-4</sub>alkyl)<sub>2</sub>;  
one of R<sub>b</sub>, R<sub>c</sub>, R<sub>d</sub> and R<sub>e</sub> is halogen; C<sub>1-4</sub>alkoxy; C<sub>1-4</sub>alkyl; CF<sub>3</sub> or CN and the other three

substituents are each H; or  $R_b$ ,  $R_c$ ,  $R_d$  and  $R_e$  are all H; and  
 $R$  is a radical of formula (a), (b) or (c)



wherein

$R_1$  is  $-(CH_2)_n-NR_3R_4$ ,

wherein

each of  $R_3$  and  $R_4$ , independently, is H or  $C_{1-4}$ alkyl; or  $R_3$  and  $R_4$  form together with the nitrogen atom to which they are bound a heterocyclic residue;

$n$  is 0, 1 or 2; and

$R_2$  is H; halogen;  $C_{1-4}$ alkyl;  $CF_3$ ; OH; SH;  $NH_2$ ;  $C_{1-4}$ alkoxy;  $C_{1-4}$ alkylthio;  $NHC_{1-4}$ alkyl;  $N(di-C_{1-4}alkyl)_2$ , CN, alkyne or  $NO_2$ ;

wherein

each of  $R_{10}$  and  $R_{10a}$ , independently, is a heterocyclic residue; or a radical of formula  $\alpha$



wherein  $X$  is a direct bond, O, S or  $NR_{11}$  wherein  $R_{11}$  is H or  $C_{1-4}$ alkyl,

$R_f$  is  $C_{1-4}$ alkylene or  $C_{1-4}$ alkylene wherein one  $CH_2$  is replaced by  $CR_xR_y$  wherein one of  $R_x$  and  $R_y$  is H and the other is  $CH_3$  each of  $R_x$  and  $R_y$  is  $CH_3$  or  $R_x$  and  $R_y$  form together  $-CH_2-CH_2-$ ,

$Y$  is bound to the terminal carbon atom and is selected from OH,  $-NR_{30}R_{40}$  wherein each of  $R_{30}$  and  $R_{40}$ , independently, is H,  $C_{3-6}$ cycloalkyl,  $C_{3-6}$ cycloalkyl- $C_{1-4}$ alkyl, aryl- $C_{1-4}$ alkyl, heteroaryl- $C_{1-4}$ alkyl,  $C_{2-6}$ alkenyl or  $C_{1-4}$ alkyl optionally substituted on the terminal carbon atom by OH, halogen,  $C_{1-4}$ alkoxy or  $-NR_{50}R_{60}$  wherein each of  $R_{50}$  and  $R_{60}$ , independently, is H,  $C_{1-4}$ alkyl,

C<sub>3-6</sub>cycloalkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl, aryl-C<sub>1-4</sub>alkyl, or R<sub>30</sub> and R<sub>40</sub> form together with the nitrogen atom to which they are bound a heterocyclic residue; and each of R<sub>20</sub> and R<sub>20a</sub>, independently, is H; halogen; C<sub>1-4</sub>alkyl; C<sub>1-4</sub>alkoxy; CF<sub>3</sub>; nitrile; nitro or amino; or a salt thereof.

Claim 6. (Withdrawn): A compound according to claim 5 wherein R<sub>a</sub> is H or methyl; each of R<sub>2</sub>, R<sub>20</sub> and R<sub>20a</sub>, independently, is H, Cl, NO<sub>2</sub>, F, CF<sub>3</sub> or methyl, n is 0 or 1; one of R<sub>b</sub>, R<sub>c</sub>, R<sub>d</sub> and R<sub>e</sub> is methyl or ethyl and the other three substituents are H; or R<sub>b</sub>, R<sub>c</sub>, R<sub>d</sub> and R<sub>e</sub> are all H; and each of R<sub>3</sub> and R<sub>4</sub>, independently, is H, methyl, ethyl or *i*-propyl; or R<sub>3</sub> and R<sub>4</sub> form together with the nitrogen atom to which they are bound a heterocyclic residue optionally substituted; and each of R<sub>1</sub>, R<sub>10</sub> and R<sub>10a</sub>, independently, is a heterocyclic residue.

Claim 7. (Currently amended): A compound according to claim 5 which is selected from  
3-[5-Chloro-2-(4-methyl-piperazin-1-yl)-pyridin-4-yl]-4-(1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(7-Aminomethyl-2-Chloro-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(6-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(5-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;  
3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7- dimethylaminomethyl-naphthalen-1-yl)-4-(6-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7- dimethylaminomethyl-naphthalen-1-yl)-4-(5-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-{2-Chloro-7-[(ethyl-methyl-amino)-methyl]-naphthalen-1-yl}-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-diethylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-ethylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-[2-Chloro-7-(isopropylamino- methyl)-naphthalen-1-yl]-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-[2-Chloro-7-(4-methyl-piperazin-1-ylmethyl) naphthalen-1-yl] -4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7- pyrrolidin-1-ylmethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl-naphthalen-1-yl)-4-(1,7-dimethyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl -naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl -naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl -naphthalen-1-yl)-4-(1-H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Amino-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Amino-naphthalen-1-yl)-4-(1H -indol-3-yl)-pyrrole-2,5-dione;

3-(7-Dimethylaminomethyl-2-fluoro-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-dimethylaminomethyl-2-fluoro-naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;

3-(1-Methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-pyrrole-2,5-dione;

3-(7-methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-trifluoromethyl-pyridin-3-yl]-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-trifluoromethyl-pyridin-3-yl]-pyrrole-2,5-dione;

3-(1-methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-trifluoromethyl-pyridin-3-yl]-pyrrole-2,5-dione;

3-(7-methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-nitro-pyridin-3-yl]-pyrrole-2,5-dione;

3-[2-chloro-5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-4-[5-methyl-2-(4-methyl-piperazin-1-yl)-pyridin-4-yl]-pyrrole-2,5-dione;

3-(1H-indol-3-yl)-4-[2-(4-methyl-piperazin-1-yl)-5-nitro-pyridin-4-yl]-pyrrole-2,5-dione; and

3-(1H-indol-3-yl)-4-[2-(4-methyl-piperazin-1-yl)-5-trifluoromethyl-pyridin-4-yl]-pyrrole-2,5-dione;

in free form or in a pharmaceutically acceptable salt form.

Claim 8. (Withdrawn): A compound according to claim 5, in free form or in a pharmaceutically acceptable salt form, for use as a pharmaceutical.

Claim 9. (Withdrawn): A compound according to claim 2, for treating or preventing diseases or disorders mediated by T lymphocytes and/or PKC, in particular allograft rejection, graft versus host disease, autoimmune diseases, infectious diseases, inflammatory diseases, cardiovascular diseases or cancer.

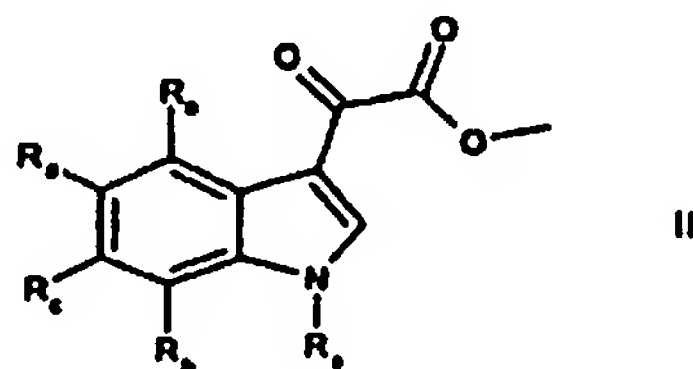
Claim 10. (Withdrawn): A pharmaceutical composition comprising a compound according to claim 2, in free form or in pharmaceutically acceptable salt form, in association with a pharmaceutically acceptable diluent or carrier therefor.

Claim 11. (Canceled)

Claim 12. (Withdrawn): A pharmaceutical combination comprising a compound according to claim 2, in free form or in a pharmaceutically acceptable salt form, and a further agent selected

from immunosuppressant, immunomodulatory, anti-inflammatory, chemotherapeutic, antiproliferative and anti-diabetic agents.

Claim 13. (Withdrawn): A process for the production of a compound according to claim 5, which process comprises reacting a compound of formula II



wherein  $R_a$  to  $R_e$  are as defined in claim 5,

with a compound of formula III



wherein R is as defined in claim 5,

and, where required, converting the resulting compound of formula I obtained in free form to a salt form or vice versa, as appropriate.

Claim 14. (Withdrawn): A method for treating or preventing disorders or diseases mediated by T lymphocytes and/or PKC, in particular allograft rejection, graft versus host disease, autoimmune diseases, infectious diseases, inflammatory diseases, cardiovascular diseases or cancer, in a subject in need of such a treatment, which method comprises administering to said subject an effective amount of an inhibitor of PKC which possesses a selectivity for PKC $\alpha$ , PKC $\beta$  and optionally PKC $\theta$ , over one or more of the other PKC isoforms of at least 10 fold, as measured according to claim 2, or a pharmaceutically acceptable salt thereof.

Claim 15. (Withdrawn): A method for treating or preventing disorders or diseases mediated by T lymphocytes and/or PKC, in particular allograft rejection, graft versus host disease, autoimmune diseases, infectious diseases, inflammatory diseases, cardiovascular diseases or cancer, in a subject in need of such a treatment, which method comprises administering to said subject an effective amount of a compound according to claim 2, or a pharmaceutically acceptable salt thereof.